

## Online Resource 2

Journal: Pharmaceutical Research

Title: Application of pharmacokinetic-pharmacodynamic modeling to inform translation of *in vitro* NaV1.7 inhibition to *in vivo* pharmacological response in non-human primate

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<sup>2</sup> In Vivo Neuropharmacology

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<sup>4</sup> Neuronal Signaling

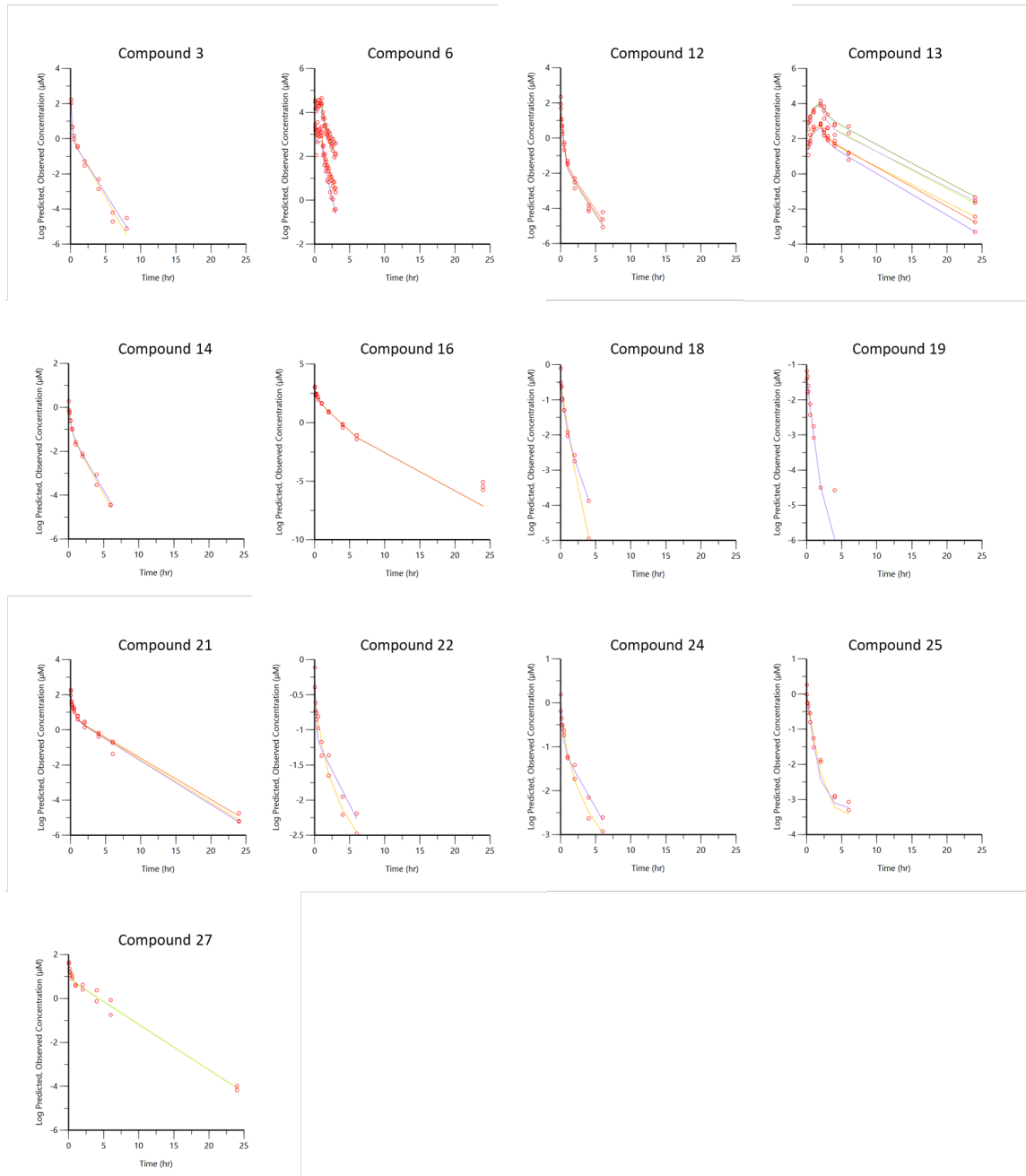
<sup>5</sup> Quantitative Biosciences

<sup>6</sup> Discovery Chemistry

Corresponding author: Jeanine E. Ballard

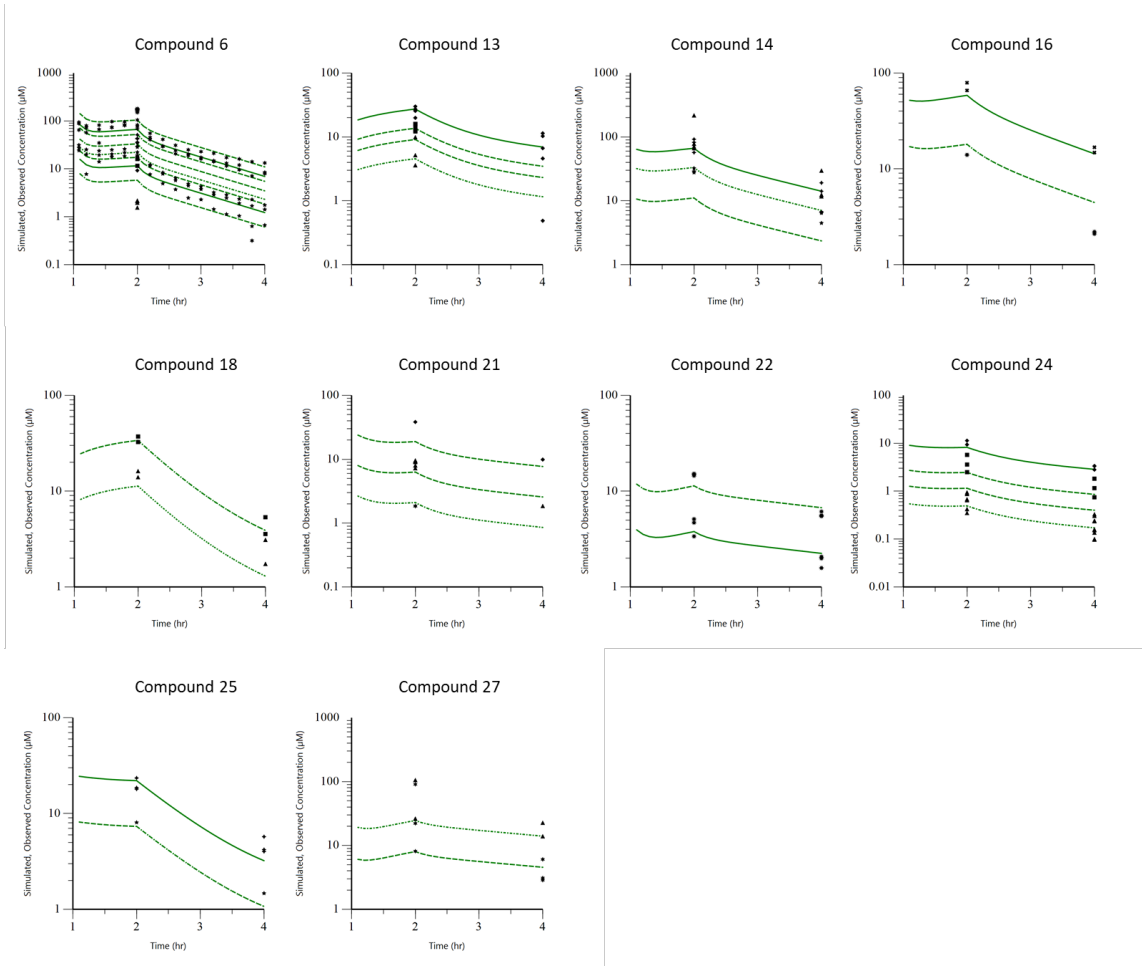
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Supplementary Figure S4. Visual predictive check of model predicted versus observed plasma concentration over time for each compound in satellite PK studies

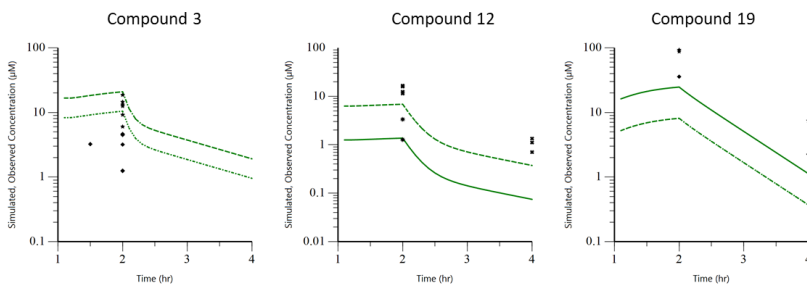


Supplementary Figure S5. Visual predictive check of simulated versus observed plasma concentration over time for each compound in fMRI PK studies

(a) Compounds with acceptable simulation of IV infusion PK profile

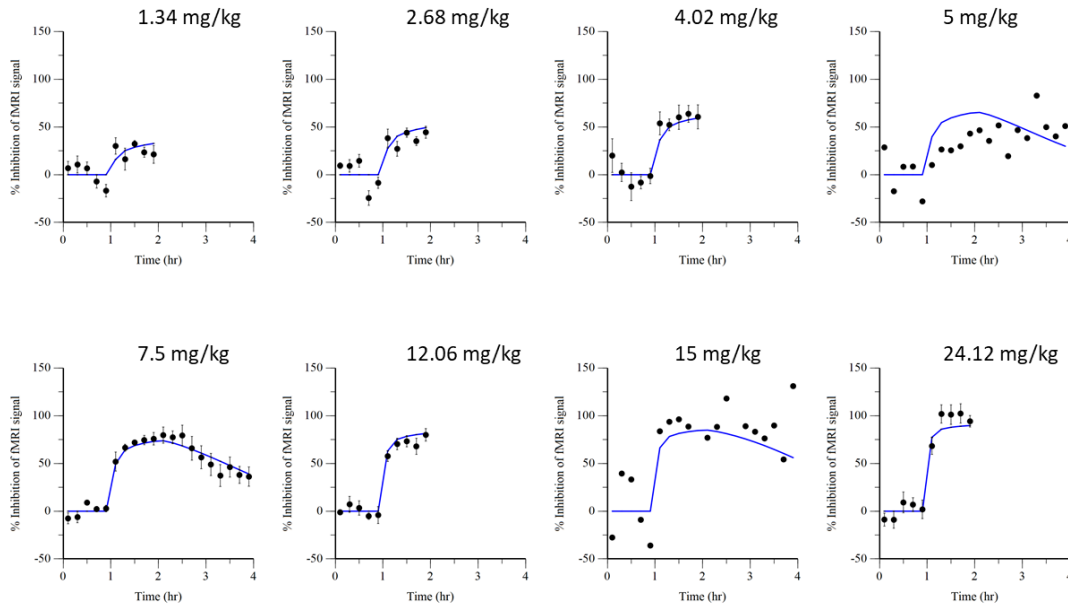


(b) Compounds with unacceptable simulation of IV infusion PK profile

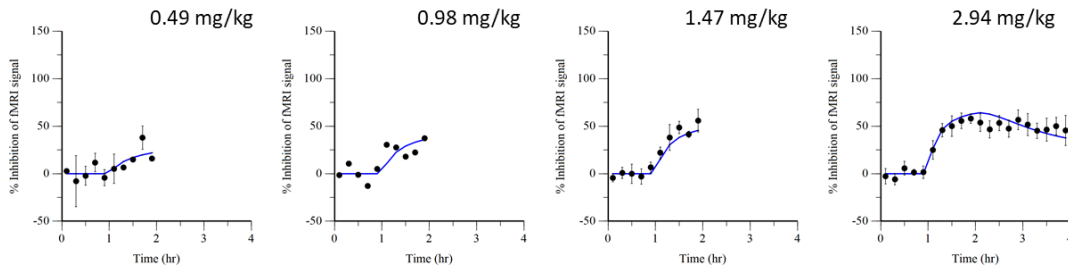


Supplementary Figure S6. Visual predictive check of effect compartment PK-PD model predicted versus observed percent inhibition of fMRI signal over time for each compound with washout data in the fMRI assay

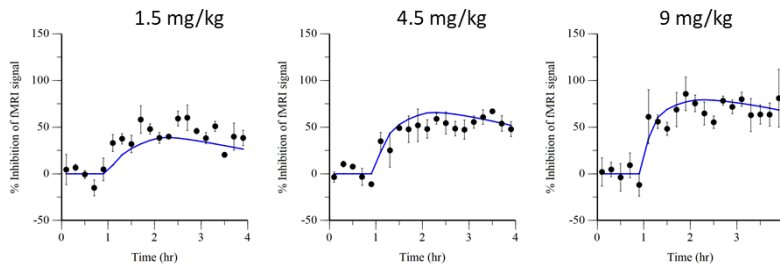
Compound 6



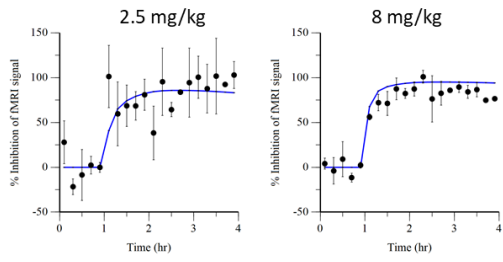
Compound 13



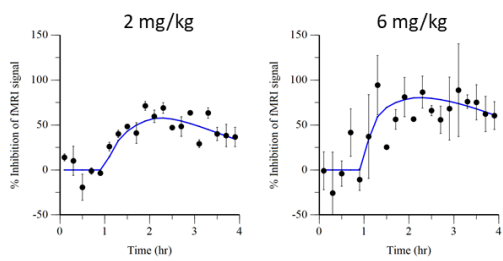
Compound 14



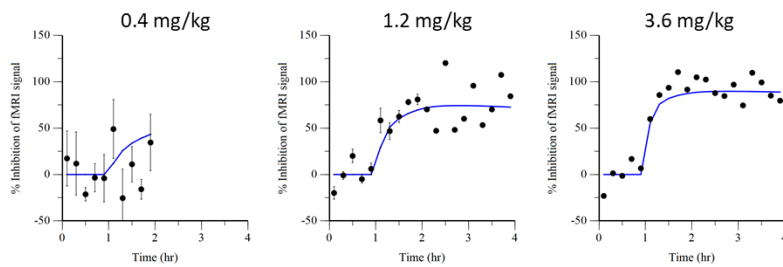
## Compound 16



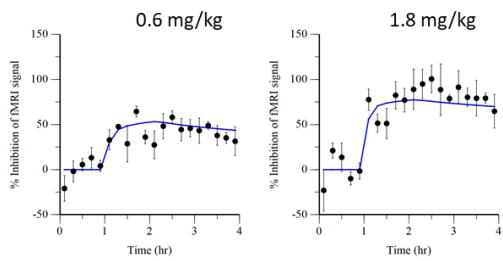
## Compound 18



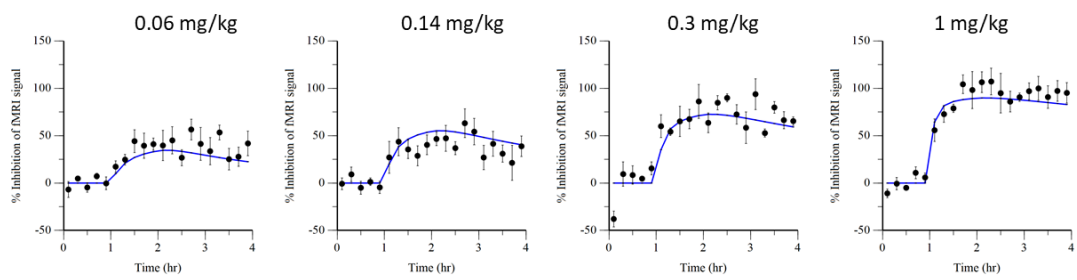
## Compound 21



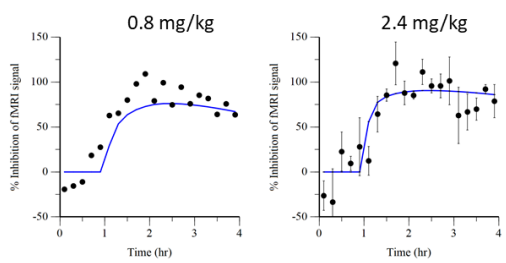
## Compound 22



## Compound 24



### Compound 25



### Compound 27

